UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/710,082	11/10/2000	Ian W. Hunter	1118/174	4206

2101 7590 05/29/2003

BROMBERG & SUNSTEIN LLP
125 SUMMER STREET
BOSTON, MA 02110-1618

EXAMINER	
SODERQUIST, ARLEN	
ART UNIT	**PAPER NUMBER**
1743	

14

DATE MAILED: 05/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/710,082	Applicant(s) Hunter
	Examiner Arlen Soderquist	Art Unit 1743

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 14, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 4-17, 41, and 44* is/are pending in the application.

4a) Of the above, claim(s) ____ is/are withdrawn from consideration.

5) ☐ Claim(s) ____ is/are allowed.

6) ☒ Claim(s) *1, 4-17, 41, and 44* is/are rejected.

7) ☐ Claim(s) ____ is/are objected to.

8) ☐ Claims ____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on ____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 11

4) ☐ Interview Summary (PTO-413) Paper No(s). ____

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other:

1. The disclosure is objected to because of the following informalities: the continuing data should be updated to show the current status of parent applications.

Appropriate correction is required.

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 1, 3-15, 41 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over de Macario (US Patent 4, 682,890) in view of Davis. In the patent de Macario describes a carrier and a microsample holder (30) for use in horizontal beam spectrophotometers in place of conventional cuvette supports that normally are used with such spectrophotometers. The microsample holder is formed as a plate having a number of retaining elements preferably in the form of a circular perforated areas for retaining drops of samples to be analyzed by the spectrophotometer. Columns 2-3 teach a sample holder of similar design is known for vertical beam spectrometers. Columns 7-8 teach that the holder (30) is formed with a set of retaining elements, such as a row of four retaining elements (32,34,36,38). The retaining elements are of circular shape having diameters on the order of about 3 mm, each retaining element being capable of retaining a 5-10 μl sample of liquid to be analyzed. The surfaces of holder (30) other than the circular areas may be coated with a thin layer of hydrophobic material to assure retention of the liquid samples within the circular areas. The circular hole diameter permits the surface

tension of the liquid sample to retain that sample stably within the confines of the hole. The remainder of holder (30) need not be light transmissive, it is, nevertheless, advantageous to its construction to construct the plate of transparent material, such as glass, plastic, quartz or the like. The holder (30) may be modified within the scope of the invention to have two or more rows of retaining elements, if desired, such as the rectangular pattern shown in FIG. 5 and described in column 7, lines 45-61 or column 11, lines 6-28. It is recognized that the holder is readily usable with the normal support-receptacle and automatic or manual indexing mechanism of conventional horizontal beam spectrophotometers to pass through the center of each sample retained by retaining elements. In this respect the paragraph bridging columns 7-8 teaches that since the overall height, length and width of the carrier are identical (or substantially identical) to the height, length and width of the conventional cuvette support, the carrier is readily usable with the normal support-receptacle and automatic or manual indexing mechanism of conventional horizontal beam spectrophotometers. Thus, the retaining elements are aligned with the analyzing beam that normally passes through windows of the conventional cuvette support. It is seen that the analyzing beam thus passes through the center of each sample retained by retaining elements. The beam passes through only one sample at a time, and as the carrier is indexed, and successive samples are exposed to the beam. The patent also teaches that the de Macario device is meant to reduce the amount of sample required for the testing. The paragraph bridging columns 10-11 teaches the addition of reagents and samples to the holes of the device. The hole diameter, plate thickness and density of holes taught by de Macario are greater than claimed, however the patent also teaches that the de Macario device is meant to reduce the amount of sample required for the testing.

In the patent Davis teaches a sample support for optical observation which is similar to that taught by de Macario. The drawings show a specimen tray or holder (1) to be employed for optical observation or analysis, and in particular for use in infrared microspectroscopy. The holder (1) includes one or more openings (2) and each opening is provided with an internal ledge or shoulder (3) and a specimen support (4) is supported on each ledge. Each support is preferably a disc-like member having a pair of generally flat, parallel, opposed surfaces and one

or more unobstructed holes (5) extend through the support between the opposed surfaces. Each support is formed of a generally rigid material which will not be attacked by water or acids. Metals, such as stainless steel or gold; or plastic materials such as nylon, polytetrafluoroethylene (Teflon), or Kevlar, can be used to produce the support 4. As shown in the drawings, holes (5) are generally circular in cross section, but it is contemplated that the holes can have other cross-sectional configurations. Davis teaches that holes (5) have a diameter greater than 10 microns, generally in the range of about 10μm and 13 mm. The cross sectional area or diameter of the holes is correlated with the surface tension of a liquid specimen to be analyzed, such that a film (6) of the liquid will span or enclose the holes, as shown in figure 2. This is taught as being adjustable to provide a quality spectrum based on the thickness of the sample being investigated. Holes (5) can all be of the same diameter or cross-sectional area, or alternately as illustrated in figure 2, the holes can have different diameters. With different diameter holes, the thickness of the liquid film which bridges or encloses the holes will vary with the hole diameter, and thus the operator can select a film thickness to provide the best quality spectrum. By directing an infrared beam through the unsupported film in one of the selected holes, an infrared spectrum of the specimen can be generated. In figure 2 the distance between the two holes is shown as less than the diameter of the holes.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use smaller diameters within the range taught by Davis because of the ability to further reduce the sample volume and provide a quality spectrum using a single hole. Applicants are directed to the fact that the Courts have held the size of an article to be not a matter of invention; the discovery of an optimum value of a known result effective variable without producing any new or unexpected results is within the skill of the routineer in the art; and mere duplication of parts without any new and unexpected results is within the skill in the routineer in the art. See *In re Rose*, 105 USPQ 237 (CCPA 1955), *In re Boesch*, 205 USPQ 215 (CCPA 1980) and *In re Harza*, 124 USPQ 378 (CCPA 1960), respectively. Thus it would have been obvious to one of ordinary skill in the art at the time of the invention was made to optimize a density of holes and

hole dimensions in order to produce a film thickness that would provide a proper spectra as taught by Davis and to provide a sufficient amount of sample to detect.

4. Claims 16-17 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over de Macario in view of Davis as applied to claims 1, 3-15, 41 and 44 above, and further in view of Böcker (US 5,786,226 newly applied). de Macario does not teach an array detector.

In the patent Böcker teaches quantitative transmission spectroscopy where a sample liquid is applied onto a sample carrier having a net in such a manner that the liquid spreads across the meshes of the net. The liquid on the net is exposed to radiation essentially perpendicularly to the net, and the transmitted radiation is detected. The net accomplishes a dosing of the liquid in such a manner that identical meshes include identical quantities of liquid. For a given net, it is possible to derive the amount of liquid, which is located in a mesh and accessible to radiation, from a net constant. Knowing the amount of liquid detected by the radiation, it is possible to use the radiation absorption to calculate the concentration of one or several analytes contained in the sample liquid. In column 5 lines 23-36, Böcker teaches the detection of samples in the filled meshes. The net of a sample carrier can be scanned with a light beam which is smaller than the cross section of the meshes similar to the detection method of de Macario. Detecting the transmitted light beam allows differentiating between liquid-filled and non-filled meshes. Advantageously, image recognition can be accomplished with a method where a light beam of a sufficient size is directed onto the net, and the transmitted radiation is detected with a CCD array. Based on the signals generated by the CCD array and using known algorithms for pattern detection, it is possible to distinguish between filled and unfilled meshes and to determine the number of filled meshes.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the detector array of Böcker in the de Macario method because of the ability to use the detected signal to determine multiple sample containing positions without scanning which Böcker teaches as an advantage.

5. Claims 1, 3-17, 41 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over de Macario (US Patent 4, 682,890) in view of Davis and Modlin or Stylli (last two newly cited

and applied). In the patent de Macario describes a carrier and a microsample holder (30) for use in horizontal beam spectrophotometers in place of conventional cuvette supports that normally are used with such spectrophotometers. The microsample holder is formed as a plate having a number of retaining elements preferably in the form of a circular perforated areas for retaining drops of samples to be analyzed by the spectrophotometer. Columns 2-3 teach a sample holder of similar design is known for vertical beam spectrometers. Columns 7-8 teach that the holder (30) is formed with a set of retaining elements, such as a row of four retaining elements (32,34,36,38). The retaining elements are of circular shape having diameters on the order of about 3 mm, each retaining element being capable of retaining a 5-10 μl sample of liquid to be analyzed. The surfaces of holder (30) other than the circular areas may be coated with a thin layer of hydrophobic material to assure retention of the liquid samples within the circular areas. The circular hole diameter permits the surface tension of the liquid sample to retain that sample stably within the confines of the hole. The remainder of holder (30) need not be light transmissive, it is, nevertheless, advantageous to its construction to construct the plate of transparent material, such as glass, plastic, quartz or the like. The holder (30) may be modified within the scope of the invention to have two or more rows of retaining elements, if desired, such as the rectangular pattern shown in FIG. 5 and described in column 7, lines 45-61 or column 11, lines 6-28. It is recognized that the holder is readily usable with the normal support-receptacle and automatic or manual indexing mechanism of conventional horizontal beam spectrophotometers to pass through the center of each sample retained by retaining elements. In this respect the paragraph bridging columns 7-8 teaches that since the overall height, length and width of the carrier are identical (or substantially identical) to the height, length and width of the conventional cuvette support, the carrier is readily usable with the normal support-receptacle and automatic or manual indexing mechanism of conventional horizontal beam spectrophotometers. Thus, the retaining elements are aligned with the analyzing beam that normally passes through windows of the conventional cuvette support. It is seen that the analyzing beam thus passes through the center of each sample retained by retaining elements. The beam passes through only one sample at a time, and as the carrier is indexed, and successive samples are exposed to the

beam. The patent also teaches that the de Macario device is meant to reduce the amount of sample required for the testing. The paragraph bridging columns 10-11 teaches the addition of reagents and samples to the holes of the device. The hole diameter, plate thickness and density of holes taught by de Macario are greater than claimed, however the patent also teaches that the de Macario device is meant to reduce the amount of sample required for the testing.

In the patent Davis teaches a sample support for optical observation which is similar to that taught by de Macario. The drawings show a specimen tray or holder (1) to be employed for optical observation or analysis, and in particular for use in infrared microspectroscopy. The holder (1) includes one or more openings (2) and each opening is provided with an internal ledge or shoulder (3) and a specimen support (4) is supported on each ledge. Each support is preferably a disc-like member having a pair of generally flat, parallel, opposed surfaces and one or more unobstructed holes (5) extend through the support between the opposed surfaces. Each support is formed of a generally rigid material which will not be attacked by water or acids. Metals, such as stainless steel or gold; or plastic materials such as nylon, polytetrafluoroethylene (Teflon), or Kevlar, can be used to produce the support 4. As shown in the drawings, holes (5) are generally circular in cross section, but it is contemplated that the holes can have other cross-sectional configurations. Davis teaches that holes (5) have a diameter greater than 10 microns, generally in the range of about 10μm and 13 mm. The cross sectional area or diameter of the holes is correlated with the surface tension of a liquid specimen to be analyzed, such that a film (6) of the liquid will span or enclose the holes, as shown in figure 2. This is taught as being adjustable to provide a quality spectrum based on the thickness of the sample being investigated. Holes (5) can all be of the same diameter or cross-sectional area, or alternately as illustrated in figure 2, the holes can have different diameters. With different diameter holes, the thickness of the liquid film which bridges or encloses the holes will vary with the hole diameter, and thus the operator can select a film thickness to provide the best quality spectrum. By directing an infrared beam through the unsupported film in one of the selected holes, an infrared spectrum of the specimen can be generated. In figure 2 the distance between the two holes is shown as less than the diameter of the holes.

In the patent Modlin teaches a high-throughput light detection instrument and method. Confocal optics structure enables exclusive light detection from a sensed volume in a composition. Columns 1-3 discuss the use of libraries in the drug discovery process and the benefit of large libraries. In particular column 3, lines 12-35 discuss the need to conserve reagents to reduce the screening costs and the use of microplate formats having well densities as high as 9600 wells (96-9600) on a standard sized microplate. Figure 2 shows the difference in spacings. In the paragraph bridging columns 5-6 Modlin teaches the invention provides an analyzer that enables a wide range of assay formats which can be carefully selected and fine-tuned for screening desired targets with acceptable quality and reliability, while also allowing assays to be run in smaller containers with reduced volumes. These objectives are met, in part, by employing an optical system that minimizes sample interfacial boundary interference, thereby permitting reduction in assay volume in existing formats such as 96 or 384 well plates, and utilization of denser formats such as 768, 1536, 3456, or 9600 well plates. The analyzer also enables assay flexibility by providing the capability of automatically switching between different modes, including photoluminescence, photoluminescence polarization, time-resolved photoluminescence, photoluminescence lifetime, and chemiluminescence modalities. Column 10 lines 25-39 teach detectors including photomultiplier tubes, photodiodes and charge-coupled devices (CCD).

In the patent Stylli teaches systems and methods that utilize automated and integratable workstations for identifying chemicals having useful activity. The invention is also directed to chemical entities and information (e.g., chemical or biological activities of chemicals) generated or discovered by operation of workstations. The automated workstations are programmably controlled to minimize processing times at each workstation and can be integrated to minimize the processing time of the liquid samples from the start to finish of the process. Column 9, lines 8-35 teach it will be advantageous to reduce the volume of the chemical or sample processed because liquid sample processing times benefit from volume reduction as liquid dispensing times are reduced, liquid aspiration times are reduced, diffusion times after addition of a reagent or sample are decreased, temperature control of a smaller volume is more uniform and consumable

costs are greatly reduced. To reduce reagent (or chemical) volumes and permit dilution into smaller samples, the sample distribution module can include a liquid handler that comprises a plurality of nanoliter dispensers that can individually dispense a predetermined volume of less than approximately 2,000 nanoliters of liquid from a predetermined selection of addressable chemical wells into a predetermined selection of addressable sample wells. Preferably, nanoliter dispensers can dispense less than approximately 500 nanoliters, more preferably less than approximately 100 nanoliters, and most preferably less than approximately 25 nanoliters. Dispensing below 25 nanoliters can be accomplished by dispensers described by Stylli. Preferred, minimal volumes dispensed are 5 nanoliters, 500 picoliters, 100 picoliters, 10 picoliters. Preferably, a liquid handler comprises a plurality of nanoliter dispensers that can individually dispense a predetermined volume of liquid from a predetermined selection of addressable chemical wells into a predetermined selection of addressable sample wells. The nanoliter dispensers will typically have a center-to-center distance between each nanoliter dispenser of less than 9.0 mm. This feature permits liquid handling in conjunction with a variety of plate formats. Different types of nanoliter and picoliter dispensers can be used as described and known in the art, as well as such dispensers developed in the future. In one embodiment, the liquid handler can comprise a plurality of nanoliter dispensers that can individually dispense a predetermined volume. Typically, dispensers are arranged in two-dimension array to handle plates of different well densities (e.g., 96, 384, 864 and 3,456). Column 15 line 14 to column 16 line 10 teach a plate stacker used as a plate buffer. Typically, a plate stacker will up/down stack plates of a standard footprint and with different densities which are taught as including 96, 384, 864, and 3,456 well number formats (spacings of ~ 1cm to 1mm) or greater (e.g., 6,912 or 13,024, spacings of less than 1mm)). The operation of the sample distribution module will usually be highly flexible to satisfy the needs of different liquid processing applications. Predefined operations can be made available for selection by an end user, or end users may create an entirely new method. Operations can be performed on a wide variety of plates and batch sizes of plates can vary. Sample plates and chemical plates may be selected with a different format from distribution plates (e.g., daughter plates). The sample distribution module will typically

provide for a stand alone mode and can be preferably integrated with a data processing and integration module.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use smaller diameters within the range taught by Davis because of the ability to further reduce the sample volume and provide a quality spectrum using a single hole and thereby provide the cost and time advantages taught by Modlin and Stylli. Applicants are directed to the fact that the Courts have held the size of an article to be not a matter of invention; the discovery of an optimum value of a known result effective variable without producing any new or unexpected results is within the skill of the routineer in the art; and mere duplication of parts without any new and unexpected results is within the skill in the routineer in the art. See *In re Rose*, 105 USPQ 237 (CCPA 1955), *In re Boesch*, 205 USPQ 215 (CCPA 1980) and *In re Harza*, 124 USPQ 378 (CCPA 1960), respectively. Thus it would have been obvious to one of ordinary skill in the art at the time of the invention was made to optimize a density of holes and hole dimensions in order to produce a film thickness that would provide a proper spectra as taught by Davis and to provide a sufficient amount of sample to detect. It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the detector arrays of Modlin and Stylli in the de Macario method because of the ability to use the detected signal to determine multiple sample containing positions without scanning since the Modlin and Stylli references clearly show that the art of analysis devices had developed to the point that signal can be detected from wells spaced at the level required by the claims.

6. Applicant's arguments and declaration under 37 CFR 1.132 filed April 14, 2003 have been fully considered but they are not persuasive. Relative to the de Macario reference examiner agrees that the reference does not anticipate the claims and has not used it as such. When the reference is considered in combination with the secondary references examiner does not come to the conclusion of applicant. In de Macario there is a clear teaching using the circular holes in a plate to replace the tubes or wells that were presently in use at the time of the reference. This included modifying the device to have minimally two, three or more rows of through-holes (see column 11). While a method of handling two rows is taught, three rows could not be handled in

the same manner which points to one of skill in the art being capable of handling three or more rows. The Courts have held that one of skill in the art is not without skill (*In re Sovish*, 226 USPQ 771 (Fed. Cir. 1985)). The level of one skilled in the art, albeit not specifically defined due to its transient nature, encompasses at least engineering logic and common sense logic applicable in the art in addition to those disclosed in the prior art references. Thus the Courts have held that one of ordinary skill in the art is capable of using engineering logic to modify methods beyond that which is taught in a reference (i.e. handling the taught three or more row plate taught by de Macario during analysis when de Macario only teaches how to handle two rows). Relative to the obviousness rejection, applicant is directed the fact the de Macario reference clearly teaches placing different samples in the different openings. Thus that is not a feature that there is a need to be taught in the secondary references and the major difference between the device and method of de Macario and the instant claims is one of the size and spacing of the through-holes. Thus the question becomes what is the size/spacing available for through-holes intended to retain liquids for analysis and the capability of analytical instruments to perform the analysis. In this respect the Davis reference clearly teaches through-holes intended to retain liquid a scale that includes both the size taught by de Macario and that required by the instant claims. Since de Macario clearly teaches a coating of a hydrophobic material around the holes to assure retention of the liquid within the hole (column 7, lines 12-16), one of skill in the art would have recognized or expected holes in the de Macario plate of the size taught by Davis to be capable of retaining different liquids within each hole if as in de Macario the amount of sample placed in each hole did not exceed the volume of the hole. Additionally, figure 2 of Davis does not show the liquid overflowing the through-hole, but is clearly contained within the through-holes . At least one of the instant independent claims and its dependent claims place a first sample in a plurality of holes through a process that is identical or substantially similar to that of Davis in that at least one liquid can be added to more than one hole (also see page 7, lines 16-22 of the instant specification). Although the de Macario device is taught as intended to replace the conventional cuvette, the paragraph bridging columns 7-8 teaches that the retaining elements (holes) are positioned that they can be index either manually

or automatically to present each of the retaining elements to the analysis beam of the spectrometer. This in combination with figure 5, column 7, line 45-61, and column 11, lines 6-28 of the de Macario patent, teaching that modifications include a two dimensional array of individual samples having "two, three or more rows of retaining elements" clearly show that de Macario contemplated more than the simple two row embodiment shown in figure 5. Additionally with either manual or automatic indexing, the amount of movement during the indexing step is not specified or limited in any manner by the patent. While the preferred spacings are such that the conventional cuvette holder can be replaced with a device that does not require modification of the spectrometer, the modifications clearly go beyond simply placing the new device in the existing spectrometer and running samples as in the prior art. The above discussed three or more row modification is a clear example of this. Thus spacings taught in the Davis patent are inclusive of at least a portion of the teachings of de Macario. The range of hole diameters taught by Davis completely encompasses the hole diameters taught by de Macario and the instant specification. Further the Davis patent which is subsequent to the de Macario patent shows that spectrometers had developed to the point that a single hole in an array of the sizes taught by Davis could be analyzed by that time. This clearly shows that by the time of Davis the art had developed to the point that the teachings of de Macario could be applied on a scale which was smaller than at the time of the de Macario patent. The secondary references are clearly within the scope of analogous art and as such provide reasons in combination with the de Macario patent for their use in the manner in which they have been applied.

Relative to claim 16, the Böcker reference teaches that use of a CCD array is advantageous compared to scanning over a two-dimensional array of sample filed openings (meshes).

While examiner believes that the above combinations clearly show the obviousness of the claimed invention the new combination of references including the Modlin and Stylli references has been added to show that the miniaturization is known to have advantages in cost and time due to the use of smaller volumes. Additionally these new references clearly show the capabilities of analysis instruments to handle arrays of individual sample containing wells on a

scale that is substantially closer to the minimum dimensions taught by Davis. Since that the though-holes of de Macario were intended to replace wells of this type, these references clearly show that the art had moved toward miniaturization and would have recognized the advantages of further miniaturization of the de Macario teachings to even smaller dimensions such as those in the Davis reference for through-hole intended to retain sample liquids. These two newly cited and applied references also are relevant to the Brenan declaration showing that multi-well plates were known at densities of 9,600 or even 13,024 wells in the same size as the standard 96-well microtiter plate. Furthermore they show that this density of wells was known or taught as early as 1997. The standard for obviousness is not what is commercially available, rather what is taught by the art. Thus the declaration is not persuasive because it does not use the proper standard for evaluating the obviousness of the combination. Additionally column 7, lines 16-23 teach that the preferable form of the de Macario plate is a perforated web (mesh) in which sample is held in the holes by surface tension. Thus de Macario teaches the placement of individual sample in holes of a perforated web (mesh) in contradiction to the statements by Doctor Brenan regarding placement of distinct samples in a mesh.

7. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The additionally cited art relates to microplates having well densities up to 9,600 and sample placement on surfaces at spacings less than 400 μm.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arlen Soderquist whose telephone number is (703) 308-3989. The examiner's schedule is variable between the hours of about 5:30 AM to about 5:00 PM on Monday through Thursday and alternate Fridays.

For communication by fax to the organization where this application or proceeding is assigned, (703) 305-7719 may be used for official, unofficial or draft papers. When using this number a call to alert the examiner would be appreciated. Numbers for faxing official papers are 703-872-9310 (before finals), 703-872-9311 (after-final), 703-305-7718, 703-305-5408 and 703-305-5433. The above fax numbers will generally allow the papers to be forwarded to the examiner in a timely manner.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.

Arlen Soderquist May 28, 2003
ARLEN SODERQUIST
PRIMARY EXAMINER